

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method of determining the binding site specificity of ~~an~~ analyte a first analyte that binds to a ligand having at least two different binding sites, comprising:

immobilizing the ligand to a sensing surface of a biosensor,

providing a second, reference analyte which binds reversibly to the ligand at a binding site thereof and which is selected to have a dissociation phase, after interaction with the ligand has ceased, that is either substantially faster or substantially slower than that of the first analyte,

contacting a mixture of the first analyte and the second, reference analyte with the immobilized ligand to permit association to the ligand,

stopping the contacting of the first analyte and the second, reference analyte with the ligand, and subjecting the immobilized ligand to conditions which permit dissociation of bound first analyte and second, reference analyte therefrom,

monitoring in real time by a label-free detection technique at least the dissociation phase of the interaction of the mixture of the first analyte and the second, reference analyte with the immobilized ligand to obtain a dissociation phase binding curve,

successively increasing the concentration in the mixture of the one of the first analyte and the second, reference analyte that has the faster dissociation phase, and

determining, from a label-free detection technique, the influence of the increased concentration on the dissociation phase binding curve profile of the mixture to determine therefrom if the first analyte and the second, reference analyte bind to the same or different binding sites on the ligand,

wherein an influence in which a substantially reduced contribution to the dissociation phase binding curve profile for the mixture from the one of the first analyte and the second, reference analyte that has the slower dissociation phase indicates that the first analyte and the second, reference analyte bind to the same binding site.

Claim 2 (currently amended): The method according to claim 1, wherein the second, reference analyte binds to a known binding site of the ligand.

Claims 3-4 (cancelled)

Claim 5 (currently amended): The method according to claim 1, wherein the second, reference analyte has a faster dissociation phase than that of the first analyte.

Claim 6 (currently amended): The method according to claim 5, wherein the association and dissociation phases of the second, reference analyte are represented by a square wave type binding curve, and the association and dissociation phases of the first analyte are represented by a binding curve having visible association and dissociation phases.

Claim 7 (currently amended): The method according to claim 1, wherein the second, reference analyte has a slower dissociation phase than that of the first analyte.

Claim 8 (currently amended): The method according to claim 7, wherein the association and dissociation phases of the first analyte are represented by a square wave type binding curve, and the association and dissociation phases of the second, reference analyte are represented by a binding curve having visible association and dissociation phases.

Claim 9 (cancelled)

Claim 10 (original): The method according to claim 1, wherein the method is repeated with at least one other reference analyte that binds specifically to a different binding site on the ligand.

Claim 11 (cancelled)

Claim 12 (previously presented): The method according claim 1, wherein the biosensor is an optical biosensor.

Claim 13 (previously presented): The method according to claim 12, wherein the biosensor is based on evanescent wave sensing.

Claim 14 (previously presented): The method according to claim 12, wherein the biosensor is based on surface plasmon resonance (SPR).

Claim 15 (currently amended): The method according to claim 1, wherein the first analyte and each of the second, and other reference analyte are contacted with the sensing surface in a flow cell.

Claim 16 (previously presented): The method according to claim 1, wherein the ligand is serum albumin.

Claim 17 (original): The method according to claim 1, wherein the ligand is a protein kinase.

Claim 18 (original): The method according to claim 1, wherein the ligand is a drug target.

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Claim 19 (original): The method according to claim 1, wherein the method is computer implemented.

Claims 20-34 (cancelled)

Claim 35 (previously presented): The method according to claim 1, wherein the ligand is human serum albumin (HSA).